


## Medical therapy versus percutaneous coronary intervention in ischemic heart disease: A cost-effectiveness analysis

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### Abstract

**Background:** Ischemic heart disease is categorized into two acute and chronic groups, and its treatments include revascularization and medical therapy. The aim of this study is to evaluate the economic burden of medical therapy compared to percutaneous coronary intervention in ischemic heart disease.

**Methods:** This study has been done in two steps. The first was a systematic review and meta-analysis to measure the effectiveness of two interventions and the second step was a cost-effectiveness analysis from the perspective of society. The data analysis included a meta-analysis and the Markov cohort simulation. RewMan v5 and tree age software were utilized. Uncertainties related to the model parameters were evaluated using one-way and two-way sensitivity analyses.

**Results:** Regarding the effectiveness of interventions, the odd ratio of the quality of life in the medical therapy group (CI: 0.76-1.10) was 0.91 times the PCI group (p=0.34). This rate for mortality in medical therapy (CI: 0.52-9.68) was 2.23 times more than the PCI group; this result was not significant (p=0.02). In the cost-effectiveness analysis, the cost-effectiveness threshold was \$ 16,482; ICER in increasing the QoL and reduction in the mortality rate was \$ 25320.11 and \$ 562.6691, respectively. Regarding the sensitivity analysis, the model was not sensitive in changing parameters in a specific domain.

**Conclusion:** According to this study, PCI is more cost-effective than medical therapy in the reduction of mortality rate and in the field of increasing quality of life. MT strategy is more cost-effective than the PCI. This study considers controversies regarding the most appropriate treatment for patients with ischemic heart disease that is helpful for health policymakers, cardiologists and health managers.

**Keywords:** Medical therapy, Percutaneous coronary intervention, Ischemic heart disease, Cost-effectiveness analysis

**Conflicts of Interest:** None declared

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### Introduction

Ischemic heart diseases are the most prevalent causes of diseases admitted in hospitals and are the second cause of mortality in Iran. Treatment cost for most of these pre-

ventable causes of readmission is remarkably high (1). Ischemic heart disease, a group of heart failure, are categorized into two acute and chronic groups, Ischemic heart

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#### ↑What is “already known” in this topic:

PCI strategy was more cost-effective in reducing mortality rate, and in the context of improving QoL, medical therapy strategy was cost-effective.

#### →What this article adds:

This study may have significant policy and clinical implications for health policymakers, cardiologists, and health managers.

disease is a condition that results from a decrease in myocardial perfusion. These diseases are often caused by coronary artery occlusion, such as atherosclerosis. Risk factors that develop ischemic heart disease are unhealthy blood cholesterol levels, hypertension, smoking, diabetes mellitus, obesity, lack of physical activity, age and so on. And complications of this disease are Chest pain, left shoulder pain, shortness of breath and weakness (2, 3).

Cardiovascular disease is one of the top 10 causes of death in the world, accounting for 25 to 45 percent of the world's mortality as the leading cause of death and the fifth leading cause of disability. 17/3 million people worldwide died in 2008 due to cardiovascular disease, which accounts for about 30% of all deaths. 80 percent of these deaths occur in poor and middle-income countries. The same death rate is expected to reach 23.6 million by 2030 (4-6). Economic evaluation of cardiovascular interventions plays an important role in decisions about reimbursement, pricing of health care, providing clinical guidance on the use of existing clinical technologies, strategic acquisition of these interventions, providing targeted health care, and generating scientific evidence to make policy decisions and ultimately allocate optimal financial resources to the health of the cardiovascular disease area (7, 8).

There are several methods for treating ischemic heart disease, which include: Medical therapy, such as the use ACE inhibitors,  $\beta$ -blockers, Angiotensin receptor blockers, Mineral corticoid receptor antagonists, Angiotensin receptor neprilysin inhibitor, diuretics, antiplatelet, and lipid regulating drugs. Coronary angioplasty or PCI method that is used to open the closed arteries of the heart. In angioplasty, a small balloon is temporarily inserted into the closed area of the artery to help widen it (9-11).

According to studies, the global cost of cardiovascular diseases in 2010 was estimated at \$ 863 billion (average per capita cost of \$ 125), which will grow by 22% to \$ 1044 billion by 2030 and it is predicted that Cardiovascular disease is a major contributor to the disability of active individuals that can severely affect the productivity of active labor force in society and reduce GDP and national income (12).

Percutaneous coronary intervention (PCI) and medical therapy are widely performed as treatment for ischemic heart disease. The cost of this interventions are much so it is essential to consider the economic evaluation of PCI and medical therapy for ischemic heart disease (7). Kodera et al concluded that in ST-elevation myocardial infarction patients, PCI was cost-effective compared to medical therapy (7); and Harindra et al concluded that In patients with stable coronary artery disease, an initial bare-metal stent (BMS) strategy is cost-effective (13). It is known that the costs of medical interventions are rising worldwide, regardless of the development of modern medical technology. Economic evaluations have been emerged as an important tool to allocate scarce resources efficiently and rationally. Methods of economic evaluations are applied to assess health care programs in many arenas containing treatments of ischemic heart disease which impose a high burden on economics worldwide (14, 15).

In this study, the costs of interventions under review are identified from the society perspective, including therapeutic and non-therapeutic direct costs and indirect costs. Our aim was to evaluate the incremental cost-effectiveness rate (ICER) of PCI and medical therapy for patients with ischemic heart disease, using a Markov decision-analytic model.

### Methods

This research has been done in two steps. The first is systematic review and meta-analysis to measure the effectiveness of PCI and medical therapy (mortality rate and quality of life), and the other is a cost-effectiveness analysis. The systematic review stage included observational and interventional studies in English and Persian language from 2000 to 2018 and examined the effectiveness of interventions in patients with ischemic heart disease. Also the quality of all studies is evaluated by the Jadad score (16); meta-analysis was done using RevMan v5 software. We analyzed the results based on the OR.  $P < 0.05$  was statistically significant (17). To test heterogeneity, the  $I^2$  test was used and because of the high heterogeneity the random effects method is used.

In the second step, a Markov model has been used to model outcomes for patients with ischemic heart disease. The cycle length was 20 years because the average age difference of patients to life expectancy in Iran is 20 years. Outcomes were a reduction in mortality and an increase in quality of life. The analysis was done from the perspective of society. All outcomes were discounted at 3% per year. Inclusion criteria were patients with ischemic heart disease with ejection fraction less than 40%. Patients were randomly assigned to a treatment group. Ethics Committee of the Iran University of Medical Sciences approved the study.

The two strategies evaluated were medical therapy and PCI. The simplified schematic of the Markov model structure is shown in Figure 1. Clinical experts' opinions and reviewing the literature (13, 18, 19) were used in order to determine the transmission probability. We arbitrarily defined an intervention "cost-effective" if it was less than three times the GDP per capita and "not cost-effective" if it was higher than three times the GDP per capita. The cost-effectiveness threshold was set according to the official dollar rate in Iran in 2018. One-way and two-way sensitivity analyses were performed on all parameters

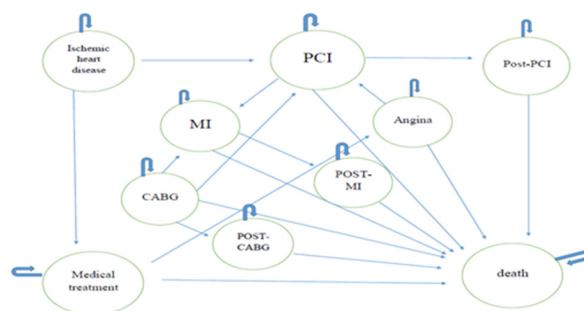


Fig. 1. Markov Decision Analysis Model

(The costs of two interventions, mortality rate, and quality of life and transition probabilities) including the discount rate from 0% to 3%.

## Results

In this study, 520 patients with ischemic heart disease were studied that 300 of them were in the PCI group and, 220 of them were in the medical therapy group. Baseline characteristics of the patients are shown in Table 1.

According to Table 1, average age was 53 and 52 years in PCI and MT interventions, respectively. The majority of patients were male (80±2). On average, 61% of patients had hypertension, and prevalence of diabetes mellitus in patients was approximately 30%, 1% of patients had dyslipidemia, In both groups, Killip class  $\geq 2$  and CCS class  $\geq 2$  were estimated at about 25% and 60% of patients had Single-vessel disease.

In the systematic and meta-analysis step, study selection procedures are followed according to the PRISMA flow diagram. Finally six full text articles were included in the final analysis (20-25). All the final studies were published between 2000 and 2018. And the random-effects model was selected. In this step experimental and control group

were include PCI and MT respectively. The results of first step are summarized in Figure 2. In the context of this indicator mortality rate in medical group in CI: 0.52-9.68 was 2.23 times the PCI group but this result was not significant in  $p=0.02$ .

Also, the results of the study in context to quality of life are shown in Figure 3. The odd ratio of quality of life in medical therapy group in CI: 0.76-1.10 is 0.91 but this result was not significant in  $p=0.34$ .

## Cost-effectiveness analysis

This study was conducted on 520 patients with ischemic heart disease in Iran's referral hospitals in 2018. The cost-effectiveness threshold was \$ 16,482 and the results of the incremental cost-effectiveness graph were analyzed based on this threshold. The cost-effectiveness plan presented in Figures 4 and 5 and the results of the cost-effectiveness of two interventions in reducing patient mortality and increasing quality of life in these patients are summarized in Table 2.

As shown in Table 2, ICER is equal to 562.66 per a unit reduction in mortality rate and Willingness to pay is \$ 16,482, as a result, both interventions are cost-effective

Table 1. Baseline characteristic

Baseline characteristic	PCI	Medical Therapy
Average age (years)	53	52
Male (%)	80	78
Hypertension (%)	62	60
Diabetes mellitus (%)	30	28
Dyslipidemia (%)	48	48
Killip class <sup>1</sup> $\geq 2$ (%)	25	26
CCS <sup>1</sup> class $\geq 2$ (%)	24	25
Single-vessel disease (%)	60	60

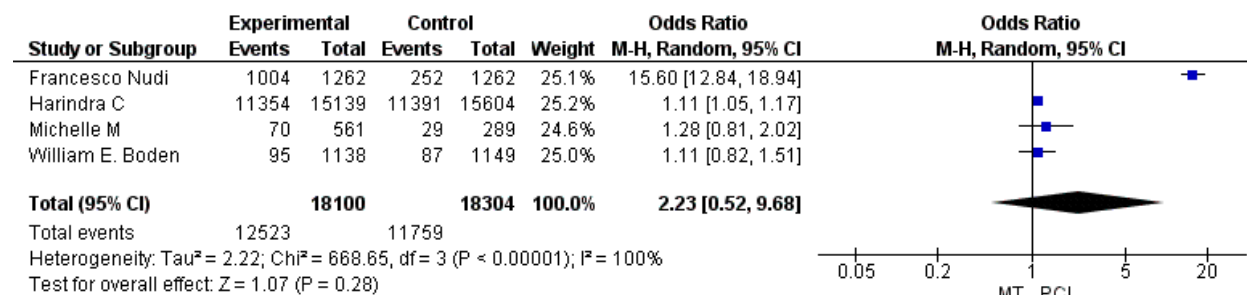


Fig. 2. Forest plot of medical therapy versus percutaneous coronary intervention in mortality rate

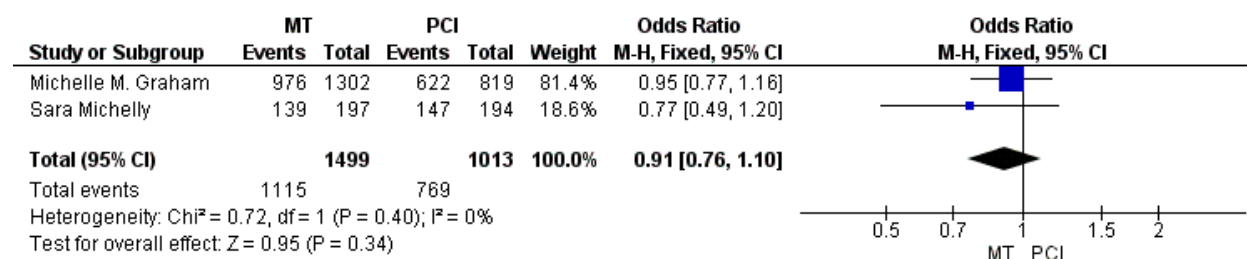


Fig. 3. Forest plot of medical therapy versus percutaneous coronary intervention in quality of life

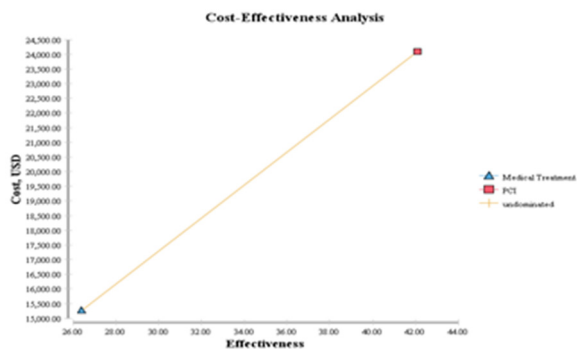


Fig. 4. Cost-Effectiveness plan for reduction in mortality rate

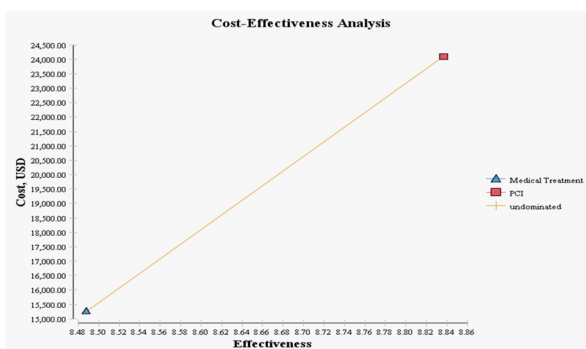


Fig. 5. Cost-Effectiveness plan for Quality of Life

but because the average cost-effectiveness of PCI is less than medical therapy, PCI strategy is more cost-effective than medical therapy. Also according to this table, ICER is equal to 25320.11 per a unit of increase in quality of life. Therefore; none of the interventions are cost-effective but since the average cost-effectiveness of medical therapy is less than PCI as a result MT strategy is more cost-effective than PCI.

**Sensitivity analysis**

In this study, first all variables related to the cost and effectiveness of two interventions were selected for sensitivity analysis using the Tornado chart. Then, the variable with the most effect on the study result was selected and, the one-way sensitivity analysis was performed on it. In mortality reduction dimension, the mortality reduction parameter in PCI strategy was selected for analysis and by doing the sensitivity analysis did not change the results of cost-effectiveness. Also in this dimension, the two-way sensitivity analysis did not change the results of cost-effectiveness (Fig. 6). According to the increasing trend in the quality of life dimension, one-way and two-way sensitivity analysis did not change the results of the cost-

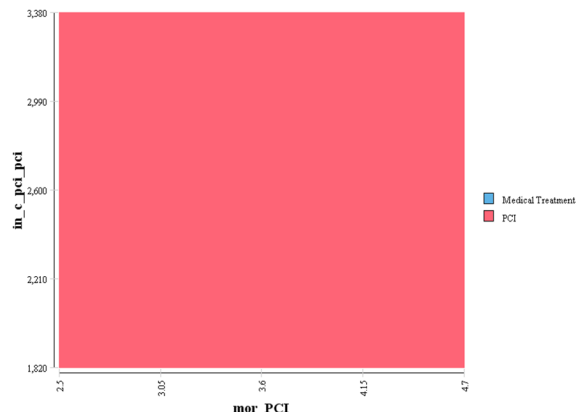


Fig. 6. Two-way sensitivity analysis for reduction in mortality rate index

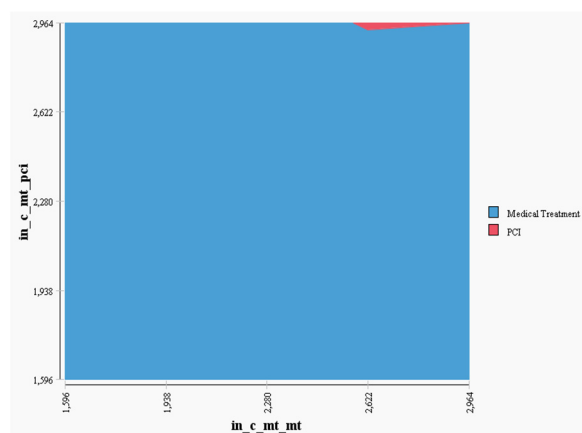


Fig. 7. Two-way sensitivity analysis for Quality of life index

effectiveness analysis (Fig. 7). Therefore, the model was not sensitive to changing parameters in a specific domain.

**Discussion**

In this cost-effectiveness analysis of medical therapy compared to PCI for ischemic heart disease, we constructed a Markov model of treatments for patients in order to compare costs and effectiveness of two interventions based on systematic review and disease costs questionnaire depend on society perspective. We performed a life-time analysis covering patient life expectancy using a long term period of 20 years. According to the results of present study, PCI strategy is more cost-effective than medical therapy in reduction of mortality rate. Gada et al (26) concluded that PCI is cost-effective in a patient with heart severe symptoms and Quality-of-life criteria, and PCI should be used more frequently than medical therapy. Wong et al (27) concluded that PCI is more cost-effective

Table 2. Cost Effectiveness Analysis

Indicator	Intervention	Cost \$	Effectiveness	Average CE	ICER	EV
Reduction in mortality	MT	15262.11	26.39372	578.2476	0	578.2476
	PCI	24094.16	42.09043	572.438	562.6691	572.438
QoL	MT	15262.11	8.487849	1798.112	0	1798.112
	PCI	24094.16	8.836665	2726.612	25320.11	2726.612

MT=medical therapy, CE= cost effectiveness, ICER= incremental cost effectiveness ratio, EV= expected value

than medical therapy in patients with severe angina. Claude J et al.(28)concluded that PCI improved clinical effectiveness at only marginally higher costs and was cost-effective; so costs should not be argued against invasive management of elderly patients with chronic angina. Kinlay S (29) concluded that from society's perspective, Percutaneous Transluminal Coronary Angioplasty (PTCA) may be more cost-effective than a medical therapy. So when percutaneous coronary intervention is used, the hospital's financial interests are best retained the use of percutaneous coronary intervention for people with private insurance can be effective. And cost-shifting may have a major impact on the provision of PCI and the costs of providing medical services need to be weighed against the cost of not providing them. The results of all these studies are consistent with the results of the present study.

This study also showed that, considering the increasing quality of life, MT strategy is more cost-effective than the PCI. Griffin et al.(30) in their study on the comparison of the effectiveness of CABG and PCI compared with medical therapy in patients with angina pectoris concluded that medical therapy was a cost-effective strategy in patients under their study. Vieira et al. (31) Concluded that in the long-term economic analysis, medical therapy was more cost-effective than Coronary Artery Bypass Grafting (CABG), and CABG was more cost-effective than PCI for patients with coronary artery disease. The strategy of PCI versus medical therapy was evaluated in the COURAGE trial, which found that PCI reduced angina symptoms and improved the quality of life at 3 years, but did not reduce the rate of death or MI. Besides that, PCI was not cost-effective compared with medical therapy (32). Hlatky et al.(33)found that medical therapy in patients with heart failure was more cost-effective compared with PCI Strategy. Ruffo showed that medical therapy dominates PTCA, allowing a greater number of patients to remain free of cardiovascular events at a lower cost (34). The results of all these studies are consistent with the results of the present study

### Conclusion

Cost-effectiveness of PCI in ischemic heart disease must be considered. If PCI does not reduce cardiovascular death or MI when added to medical therapy, it is difficult to justify the cost of PCI for asymptomatic patients. Furthermore, if PCI improves QoL, but does not reduce death, patients and payers need to know how much the cost of a period of freedom from angina is.

The main strength of this economic analysis is that it is based on systematic review and meta-analysis in the field of effectiveness data and that the cost of treating patients was calculated and analyzed from the society perspective and its main limitations were the failure to consider coronary artery bypass surgery intervention and the other limitation is the model-based design. In model-based studies, when model assumptions vary, results vary. So we set reasonable models in the present study based on previous studies and clinical experts' opinions.

This cost-effectiveness analysis of medical therapy compared to PCI found that PCI strategy was more cost-

effective in reducing mortality rate and in the context of improving QoL, medical therapy strategy was cost-effective and the high PCI consumables cost highlighted the importance of cost-effective purchasing mechanism. The present study has the following clinical implication: PCI for ischemic heart disease should be performed more often in Iran, based on its cost-effectiveness in the reduction of mortality rate. This study may have significant policy and clinical implications for health policymakers, cardiologists and health managers.

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### Conflict of Interests

The authors declare that they have no competing interests.

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